IN THE CLAIMS

Please amend the claims by amending claims 1, 4 and 5 as shown on the attached sheets, and by canceling claims 2, 6 and 7. A marked-up copy of the original text of the claims being amended is attached to this amendment. Material inserted is indicated by underlining and material deleted is indicated by enclosure in brackets.

REMARKS

Claims 1, 4 and 5 are amended to incorporate therein the limitations of claims 2, 6 and 7, respectively, and the latter three claims have been canceled as unnecessary in view of those amendments.

Double Patenting

With respect to the double patenting rejection in view of U.S. Patent 5,827,935, a terminal disclaimer will be submitted upon an indication of allowable subject matter.

35 USC §102

Reconsideration and withdrawal of the rejection of claims 1-9 under 35 USC § 102(a) as being anticipated by Sullenger (*Science*) are respectfully requested.

Sullenger (*Science*) is not available as prior art under §102. The reference was published on December 3, 1993. In contrast, the present application claims benefit under 35 USC §120 of the filing date of application Serial No. 08/185,827, now U.S. Patent 5,827,935 ("the '935 patent;" copy of front page enclosed). As is apparent from the face of the '935 patent, application Serial No. 08/185,827 was a national stage filing corresponding to PCT/US92/04362 filed May 27, 1992. Thus, under 35 USC §363 the filing date of application Serial No. 08/185,827 was May 27, 1992 (applicants' priority claim on page 1 of the application inadvertently recited the later §371 date, and is amended herein). Sullenger (*Science*) thus cannot anticipate.

Reconsideration and withdrawal of the rejection of claims 1-9 under 35 USC § 102(b) as being anticipated by Sullenger (*Cell*) are respectfully requested.

The Examiner appears to rely heavily on the statement bridging the columns on page 605 as establishing co-localization, but the statement does not prove the Examiner's point. To the contrary, Sullenger (*Cell*) states that "[t]he intracellular localization of the tRNA-TAR fusion transcripts *was not determined*" (emphasis added). The subsequent observations regarding the work of others is nothing but speculation, and there is nothing in the

Sullenger paper which would lead one of ordinary skill to believe that concentration enhancement or co-localization actually occurred. Moreover, Sullenger's inhibitor was not a ribozyme, as required in all claims.

Reconsideration and withdrawal of the rejection of claims 1-9 under 35 USC §102(e) as being anticipated by U.S. Patent 5,854,038 ("the '038 patent") are respectfully requested. The earliest possible filing date to which the '038 patent is arguably entitled is January 22, 1993. In contrast, the present application claims an effective filing date of May 27, 1992. Thus, the '038 patent is not available as prior art under 35 USC §102(e).

35 USC §112, first paragraph

Reconsideration and withdrawal of the rejection of claims 1-9 under the first paragraph of 35 USC §112 are respectfully requested. The rejection seems to be based on the contention that the specification does not enable the full scope of the claims. Specifically, the Action seems to contest that *in vivo* methods are enabled. Applicants respectfully traverse.

All claims recite methods in which concentration enhancement or co-localization between a target and an inhibitor takes place within a living cell. The Action

does not dispute that the specification provides guidance and examples demonstrating the claimed processes in living cells, but views that as limited to *in vitro* application. However, the Action fails to provide any basis for doubting that the methods taught in the specification have applicability in what the Action considers to be *in vivo* use. The specification discloses a number of methods, including viral mediated delivery (page 31, lines 21-23). The level of skill in the art is obviously quite high, and there is no evidence presented by the PTO that such a delivery system would not work in an *in vivo* setting.

Moreover, the references cited in the Action simply do not support the rejection, and the Action attributes to them an unwarranted level of importance. Agrawal, Gewirtz and Branch are all review articles which do not purport to advance any new and original research. Instead of establishing doubt as to *in vivo* use, they each report encouraging uses of the technology described in each paper.

For example, Agrawal states that:

> Over the past 2-3 years, many reports have appeared in the literature confirming the application of antisense technology in *in vivo* models . . .

Numerous reports are summarized (p. 376). Similarly, Gewirtz reports that "several [oligodeoxynucleotide] reagents have reached clinical trials for a variety of

indications, including leukemia, cancer, and AIDS" (p. 3161). Branch states that "there is growing evidence that antisense molecules can be useful pharmacological tools when applied carefully" (p. 50).

While each article does discuss the difficulties inherent in the field, they are cited as part of an academic discussion of practical considerations in the field. But the fact that certain things must be considered when designing drugs does not mean that they are insurmountable problem evidencing lack of enablement. The test is not whether *any* experimentation is necessary, but rather whether *undue* experimentation is necessary. The articles relied upon are evidence that one of ordinary skill would be given considerable guidance by the art.

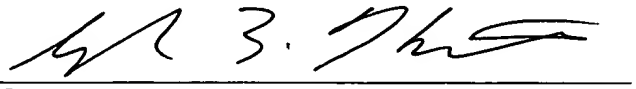
Sequence Listing

With respect to the Sequence Listing requirement, applicants note that a copy of the computer readable form was submitted on November 30, 2000 (see enclosed copy of return postcard bearing the PTO date stamp). However, enclosed herewith is a substitute copy of the computer readable form.

In accordance with 37 C.F.R. §1.821(g), I hereby state that the present submission includes no new matter.

In accordance with 37 C.F.R. §1.821(f), I hereby state that the information recorded in computer readable form is identical to the written Sequence Listing submitted on November 30, 2000.

Respectfully submitted,



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MARKED UP VERSION OF AMENDED SPECIFICATION

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part of application Serial No. 08/922,471 filed September 3, 1997, which is a continuation of application Serial No. 08/522,356 filed September 13, 1995, now abandoned; which was a continuation-in-part of application Serial No. 08/185,827 filed [January 24, 1994] May 27, 1992, now U.S. Patent No. 5,827,935.

MARKED-UP VERSION OF THE AMENDED CLAIMS

1. (amended) A process which comprises the positioning, within a living cell, of [a] an RNA target molecule and [an] a ribozyme inhibitor for said target molecule, said positioning being such that the concentration of the inhibitor molecule with respect to the target molecule is enhanced.

4. (amended) A method which comprises co-localizing [a] an RNA target molecule and [an] a ribozyme inhibitor for said target molecule within a living cell.

5. (amended) A living cell in which [a] an RNA target molecule and [an] a ribozyme inhibitor for said target molecule are co-localized.